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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,832	02/08/2005	Stephen Robert Wedge	056291-5198	3996

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EXAMINER

STONE, CHRISTOPHER R

ART UNIT	PAPER NUMBER
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1614

MAIL DATE	DELIVERY MODE
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07/11/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/523,832	Applicant(s) WEDGE, STEPHEN ROBERT	
	Examiner CHRISTOPHER R. STONE	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 April 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3, 7 and 8 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 7 and 8 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants' arguments, filed April 10 2008, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3, 7 and 8 rejected under 35 U.S.C. 103(a) as being unpatentable over Hennequin et al (WO 01/32651) in view of Gorski et al.

Claims 1-3 are drawn to a method for the treatment of cancer and a method for the production of an antiangiogenic and/or vascular permeability reducing effect in a warm-blooded animal, which comprises administering ZD6474 with an effective amount of ionizing radiation.

Hennequin et al discloses a method for the treatment of cancer, solid tumors in particular (p.28, lines 11-17), including a human non-small cell lung cancer (CaLu-6, p. 22, example c) and a method for the production of an antiangiogenic and/or vascular permeability reducing effect in a warm-blooded animal (p. 26, lines 10- 14), which comprises administering a compound of formula I (p. 3). ZD6474 is specifically identified

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as a compound of Formula I (claim 8). Hennequin et al further teaches that this treatment may additionally include radiotherapy administered simultaneously, sequentially or separately (p. 26, lines 22-30). Therefore it would have been obvious to one of ordinary skill in the art at the time of the invention to use ZD6474 with concurrent radiotherapy in the treatment of cancer and in the production of an antiangiogenic and/or vascular permeability reducing effect in a warm-blooded animal, thus resulting in the practice of the instantly claimed invention with a reasonable expectation of success. Applicant's data (Specification, pages 22-24) displays synergism between ZD6474 and sequential radiation therapy. The prior art indicates that this synergistic effect is expected. Gorski et al teaches that VEGF inhibitors, a class of compounds of which ZD 6474 is a member, administered with ionizing radiation results in greater than additive antitumor effects (p. 3378, paragraph 1).

Applicant argues that there is no motivation to combine ZD6474 with radiation therapy. This is not found to be persuasive because, as noted above, ZD6474 is explicitly disclosed in Hennequin et al as a preferred embodiment. In fact it is the only compound in claim 8. Additionally, Hennequin et al explicitly teaches that in the field of medical oncology it is normal practice to use a combination of different forms of treatment including radiotherapy and chemotherapy (p. 26, last paragraph). Applicant argues that the combination of ZD6474 and radiation produces unexpected synergistic results. This is not found persuasive because the data only demonstrates better than additive results for the sequential administration of the combination (p. 23, Table 2) and as noted above, this result is expected. Applicant argues that synergy is unexpected

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using a small molecule VEGF receptor tyrosine kinase inhibitor (ZD6474) in combination with radiation. This is found unpersuasive because Gorski et al teaches that radiation combined with an angiogenesis inhibitor, specifically a VEGF inhibitor produces better than additive antitumor activity by disrupting the VEGF signaling between the tumor and its vasculature (p. 3378, paragraph 1). A VEGF receptor tyrosine kinase inhibitor would have been expected to block this signaling at the receptor.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRISTOPHER R. STONE whose telephone number is (571)270-3494. The examiner can normally be reached on Monday-Thursday, 7:30am-4:00pm EST.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

09July2008

CRS

/Ardin Marschel/

Supervisory Patent Examiner, Art Unit 1614